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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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NOTARO, MICHALOS & ZACCARIA P.C.
100 DUTCH HILL ROAD
ORANGEBURG, NY 10962

EXAMINER	
GEMBEH, SHIRLEY V	
ART UNIT	PAPER NUMBER
1628	
MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/549,296	FRANC ET AL.	
	Examiner	Art Unit	
	SHIRLEY V. GEMBEH	1628	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *3/3/11* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,5,6 and 8-19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,5,6 and 8-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 3/3/11 has been entered.

Response to Arguments

2. The response filed 3/3/11 has been entered.

3. Applicant's arguments filed on 3/3/11 have been fully considered but they are not deemed to be persuasive.

4. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

5. Claims 1-3, 5-6 and 8-19 are pending in this office action. Claim 1 is currently amended.

6. The rejection of claims 12-19 under 35 U.S.C. 103(a) as being unpatentable over Caril et al. (US Patent US 5,275,824) in view of Zak et al. (US Patent 6,503,943) and further in view of Collaueri et al. (US Patent 6,221,393) is withdrawn in lieu of the new rejection below.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 15-19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 15 recites "…granulate is filled into a capsule or a sack or, after at least one releasing agent and/or at least one slipping agent is added to the granulate, pressed into tablets"

The claims are indefinite and unclear. It is not clear how the granulate filled into a capsule or a sack is then pressed into a tablet (with regards to instant claim 15) and/or remains smaller than 0.5 mm in size as in base claim 12.

With regards to instant claim 17 it is very confusing and unclear how the tablet surface and the surface of the granulate is filled into a capsule.

Claims 17 recites "…granulate surface, the surface of the granulate to be filled into the sack, the tablet surface and the surface of the granulate to be filled into the

capsule and/or the surface of the capsule mentioned are coated …" Claim 17 recites the limitation " granulate surface, the surface of the granulate to be filled into the sack, the tablet surface and the surface of the granulate to be filled into the capsule and/or the surface of the capsule mentioned " in claim 12. Nowhere in claims 9 and 12 is the term "surface granulate", the surface of the granulate", "the tablet surface" mentioned. There is insufficient antecedent basis for this limitation in the claim as "mentioned". The language is very confusing.

With regards to instant claim 17 it is very confusing and unclear how the tablet surface and the surface of the granulate is filled into a capsule.

Maintained Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-3, 5-6, and 8-11 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Zak et al. (US Patent 6,503,943) in view of Collaueri et al. (US Patent 6,221,393) and further in view of Caril et al. (US Patent US 5,275,824) for the reasons made of record in Paper No. 20101108 and as follows

In Summary:

Zak et al teach a pharmaceutical composition for the therapy of oncological disease containing platinum complex and at least a pharmaceutical excipient (see col. 3, lines 9-15) wherein the platinum complex is (OC-6-43) Bis(acetato)-(1-adamantylamine)-amine-dichloroplatinum (see col. 3, lines 48-51) as required by instant claim 1.

However Zak failed to teach that the formulation is by wet granulation in a tablet form with particle size smaller than 0.5 mm and fails to teach that the neutral saccharide

in an amount of at least 5% and the polysaccharide in an amount equal to at least 2% of the total weight of the granulate. Because Zak is silent of these limitations Collaueri and Caril are added to remedy the deficit.

Collaueri et al. teach a delayed release pharmaceutical composition in the form of tablets comprising polysaccharide having particles less than 100 µM which is less/smaller than 0.5 mm (as required by instant claim 1), wherein the polysaccharide is mixed with lactose (as required by instant claims 5-6, see col. 2, lines 56-61 and col. 5, lines 37-42) further comprises a sipping agent (i.e., magnesium stearate (as required by instant claim 3, see col. 3, lines 40-42). Table 1 teaches the procedure is by wetting, so therefore one of ordinary skill in the art would necessarily expect that the process is by wet granulation (see col.'s 7 and 8, as required by instant claim 1). It is also noted that the particle size is based on the release of the active agent over the desired period of time (see col. 3, lines 34-65). Collaueri also teach that the neutral saccharide is at least 20% and the polysaccharide is in an amount of at least 30% (see col. 3, lines 43-51 and col. 4, lines 8-12). Therefore the limitations of at least 5% by weight of the neutral saccharide and at least 2% by weight of the polysaccharide is taught (as recited in instant claim 2) is met. Collaueri et al. further teach that the pharmaceutical composition may be modulated to release the active agents quasi-instantaneously to slow release formulation. Therefore one of ordinary skill in the art would necessarily expect that the tablet or capsule comprises at least one pharmaceutically acceptable releasing agent (as required by instant claim 3, see col. 3, lines 66-67 bridging col. 4, lines 1-3) and thus coated with a pharmaceutically acceptable substance that enables

enterosolvent dissolution of the active substance in the bowel (as required by instant claims 8 and 9). Collaueri et al teach that the composition may comprise additional matrix such as polyethylene glycol not more than 40% (as required by instant claim 10, see col. 8, lines 42-44)

However Collaueri et al fails to teach that the compound may be (OC-6-43) Bis(acetato)-(1- adamantylamine)-amine-dichloroplatinum (as required by instant claim 1) and fails to teach instant claim 11).

Caril et al. teach therapeutic compositions with controlled release medicaments that are coated with polymeric films formed by wet granulation (see col. 4, lines 4-10) with particle size less than 0.5 mm (i.e., 100 µm, see col. 2, lines 55-56) made of HPMC (i.e., hydroxypropycellulose) or co-polymers of methacrylic (see col. 4, lines 65-67 and col. 5, lines 1-10 as required by instant claim 6) wherein the drug release formulation would reasonably expect having 0.1 mm size for delivery of drugs to the intestinal as required by instant claims 10-11).

One of ordinary skill in the art would have been motivated to expand Zak's drug composition to include Collaueri and Caril's pharmaceutical formulation of granulation with particle size less than 0.5 mm as taught by Collaueri (as discussed above) in a tablet or capsule form because Collaueri teaches that in formulating a tablet different granulate sizes are advantageous because it exhibits very good flow properties (see col. 5, lines 20-30) and the release of the active agent can be modulated in a controlled release formulation (see col. 5, lines 10-19) with high bioavailability (see Caril abstract)..

It would have been obvious to one of ordinary skill in the art to vary the amounts of matrix added to the active agent based on the release pattern taught by Collaueri. Specifically Collaueri teaches that the matrix may be in the range of 5-99% (see col. 3, lines 45-49). Therefore one of ordinary skill in the art would be motivated to expand the composition of Zak to include the teachings of Collaueri and Carli with a reasonable expectation of success in formulating a pharmaceutical composition comprising (OC-6-43) Bis(acetato)-(1- adamantylamine)-amine-dichloroplatinum having granulate size of 0.5 mm because it is advantageous because it exhibits very good flow properties (see col. 5, lines 20-30) and the release of the active agent can be modulated in a controlled release formulation (see col. 5, lines 10-19. Applicant should note that **wet granulation** is a product by process limitation. Accordingly, the courts have held that if the product in a product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior art product was made by a different process. *In re Thorpe,* 227 USPQ 964, 966 (Fed. Cir. 1985): *In re Marosi*, 218 USPQ 289, 292-293 (Fed. Cir. 1983).

This rejection is also consistent with that held by the courts in *Ex parte Gray,* 10 USPQ 2d 1922 (1989); *In re Best,* 195 USPQ 430 (CCPA 1976), which held that:

"the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product. Accordingly, since the issue in the present appeal is whether the prior art factor is identified or patently indistinct from that of the material on appeal, appellants have the burden of showing that inherency is not involved". *Ex parte Gray,* 10 USPQ 2d 1922 (1989); *In re Best,* 195 USPQ 430 (CCPA 1976).

Likewise, the courts have held that when the prior art product reasonably appears to be the same as that claimed, but differs by process in which it is produced, a rejection of this nature is eminently fair and the burden is upon the appellants to prove, by comparative evidence, a patentable difference (*In re Brown*, 173 USPQ 685 (1972)).

Thus, the claimed invention was prima facie obvious at the time of invention.

Applicant argues: that "the person of ordinary skill in the art of this invention would not combine the teachings of Zak, Collaueri and Caril, or the teachings of Caril, Zak and Collaueri as cited, to reach the claimed invention, are material for all of the claims, not just the composition claims and not just the method claims".

i) "Zak does not mention any wet granulation at all so the skilled artisan must look elsewhere for this teaching and combine it with Zak".

ii) "Collaueri does not expressly teach wet granulation either. Table 1 of this reference does not comprise anything which could be related to the wet granulation".

iii) "Carli mentions wet granulation only as an optional intermediate working step having practically no influence on the arrangement of the active ingredient in the excipient matrix".

In response: Applicant is correct that Zak did not mention wet granulation. Applicant argument that wet granulation by Collaueri was mischaracterized is considered and found persuasive, nonetheless, Caril specifically teach wet granulation

which is acknowledged by Applicant and since this is a rejection under 35 USC 103, all the cited references must be considered.

However the issue is not how the product was formed but whether the pharmaceutical composition has all the required limitation set forth in the claim and since this rejection is a rejection under 35 USC 103 all the references/prior art must be considered as a whole not in parts for what they teach. The test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference; nor is it that the claimed invention must be expressly suggested in any one or all of the references. Rather, the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981).

Again claims 1-3, 5-6, and 8-11 are drawn to a composition containing (OC-6-43)- bis(acetato)-(1-adamantylamine)-amine-dichloroplatinic platinum complex of formula (II) in a mixture with at least one pharmaceutical excipient having granulate size of 0.5 mm produced by wet granulation. Applicant should note that wet granulation is a product by process limitation. Accordingly, the courts have held that if the product in a product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior art product was made by a different process. *In re Thorpe,* 227 USPQ 964, 966 (Fed. Cir. 1985): *In re Marosi*, 218 USPQ 289, 292-293 (Fed. Cir. 1983). These claims are defined as a product-by-process claims and it is the product, not the process, that is given patentable weight (see In re Bridgeford, 357 F2d 679, 149, USPQ 5 (CCPA 1966)). It is the patentability of

the product claimed and not of the recited process steps which must be established, see In re Brown, 459 F2d 531,173 USPQ 685 (CCPA 1972); In re Wertheim, 541 F2d, 191 USPQ (CCPA 1976). A comparison of the recited process with the prior art processes does not serve to resolve the issue concerning the patentability of the product, see In re Fessman, 489 F2d 742, 180 USPQ 324 (CCPA 1974)

Applicant should note that the granulate size plays no role in a pressed tablet, because once the tablet is pressed the granulate size vanishes.

Because Zak failed to teach the limitations having at least 5% of at least one native and /or modified polysaccharide Collaueri and Carli were added to remedy the deficit. Even if Collaueri does not expressly teach wet granulation as asserted by Applicant Caril specifically teach wet granulation, additionally as already stated above the process of formulation of the product is not what is claimed.

Applicant's argument is found not persuasive for the above reasons given and already made of record.

9. Claims 12-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Caril et al. (US Patent US 5,275,824) in view of Zak et al. (US Patent 6,503,943) and Keppler et al (US 5,256,653 already of record) further in view of Collaueri et al. (US Patent 6,221,393).

The claims are directed to a method of manufacturing of the pharmaceutical composition.

Caril et al. teach process of producing a pharmaceutical composition comprising medicaments by wet granulation wherein the particle size is between 100 and 1000 µm (see col. 2, lines 40-54, thus 500 µm will equate to 0.5 mm) employing binders such as sugars (i.e., generically lactose is a sugar, see col. 4, lines 4-7) under wet condition is taught (see col. 4, lines 4-7, as required by instant claim 12). Caril additionally teaches that lactose and corn starch can be used in the wet granulation of drugs (see examples 3 -6, col.'s 7-8) thus teaches a neutral saccharide and corn starch as the native or modified polysaccharide in a tablet form (as required by instant claim 15).

In example 3 for instant Caril teaches with regards to instant claim 14, that the wet granulation is performed in an equipment, thus it is reasonable that the surfaces coming into contact with the granulated mixture are inert to the mixture(i.e., the atomization pressure is 1-1.5 bar, as required by instant claims 14 and 16)..

However Caril fails to teach that the composition comprises a platinum complex (0C-6-43) Bis(acetato)-(1- adamantylamine)-amine-dichloroplatinum in a coatings are with inert closing layer. Because Caril fails to specifically teach the compound of formula (II) Zak is added to remedy the deficiency.

Zak et al teach a pharmaceutical composition for the therapy of oncological disease containing platinum complex and at least a pharmaceutical excipient (see col. 3, lines 9-15) wherein the platinum complex is (OC-6-43) Bis(acetato)-(1-adamantylamine)-amine-dichloroplatinum (as required by instant claim 12).

Keppler et al. teach pharmaceuticals are prepared by wet mixing the active substance with the pharmaceutical vehicles that can be dispersed into capsules wherein the coatings are with inert closing layer that enables the control release of the active substance (as required by instant claims 17-19 see col. 7, lines 41-49, col. 8, lines 57-67, col. 9, lines 4-15).

Collaueri teaches with regards to instant claim 13, the concept of having varying particle size wherein the tableting preparation has at least 90% having a particle size distribution.

It would have been obvious to one of ordinary skill in the art to substitute the medicaments employed by Caril, Zak, Keppler and Collaueri with the medicament of Zak in the manufacturing of a pharmaceutical composition produced by wet granulation. One of ordinary skill in the art would have been motivated to combine the teachings of Caril, Zak, Keppler and Collaueri with a reasonable expectation that in the process of manufacturing a pharmaceutical composition with different distribution of sizes because Collaueri teaches that in formulating a tablet different granulate sizes are advantageous because it exhibits very good flow properties (see col. 5, lines 20-30) and the release of the active agent can be modulated in a controlled release formulation (see col. 5, lines 10-19).

10. No claim is allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to SHIRLEY V. GEMBEH whose telephone number is (571)272-8504. The examiner can normally be reached on 8:30 -5:00, Monday- Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, BRANDON FETTEROLF can be reached on 571-272-2919. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/SHIRLEY V GEMBEH/
Examiner, Art Unit 1628
7/5/11